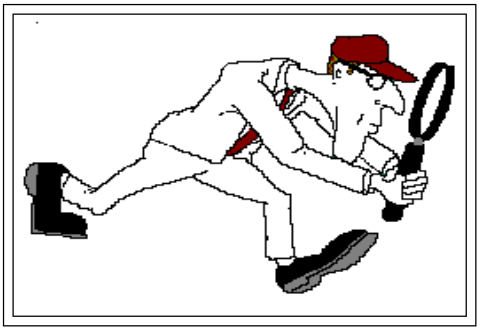
Hemophilia Surveillance System Report



Hemophilia cases identified 1993-1997 Volume 1, No. 2

Contents

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Single copies of the *Hemophilia Surveillance System Report* are available free from HANDI, the information service of the National Hemophilia Foundation by calling (800) 42-HANDI. Confidential information, referrals, and educational material on hemophilia and other bleeding disorders is also available through HANDI. The *Hemophilia Surveillance System Report* is accessible via internet at www.cdc.gov/ncidod/dastlr/Hematology.

Commentary

Hemophilia is an ancient disease which has been recognized for thousands of years. It is caused by a mutation in one of the two genes located on the x chromosome that contain the genetic code for factor VIII and factor IX -- proteins necessary for normal blood clotting. A deficiency of factor VIII is referred to as hemophilia A or "classic" hemophilia; a deficiency of factor IX characterizes hemophilia B, also known as Christmas disease. Because the defect occurs on the x chromosome (which is one of the chromosomes that determines a person's sex), almost all of the persons most severely affected by hemophilia are men.

People with hemophilia can develop serious bleeding into tissues, muscles, and joints, often without any noticeable trauma. Repeated bleeding into joints results in crippling chronic joint disease, one of the most severe complications of hemophilia. In the mid-1970's, treatment for hemophilia was improved through the use of clotting factor concentrates, products made from the plasma of donated blood. However, since thousands of blood donations are often required to obtain sufficient plasma to manufacture these products, many persons with bleeding disorders became infected with hepatitis B and C virus and human immunodeficiency virus (HIV), the virus that causes AIDS, in the early 1980s before the risk of such transmission was recognized and eliminated.

Since 1986, CDC has been involved with the hemophilia community, primarily through risk-reduction efforts aimed at preventing secondary infection of family members with hepatitis virus or HIV. In 1991, CDC received a request from the National Hemophilia Foundation to expand their collaborative hemophilia activities. Meetings with patients and hemophilia care providers were held during 1992 to determine the areas of highest priority. Based on recommendations from these constituents, a Congressional mandate was issued to CDC with the goal of reducing the human and financial burden of bleeding disorders by focusing national emphasis on prevention and early intervention. The first phase of this legislative initiative was to establish a surveillance system that would provide data on: a) the prevalence and incidence of hemophilia and its complications; b) the occurrence of complications among this population and the use of health-care resources over time; and c) the social and economic impact of hemophilia and its complications from a population perspective.

During 1993-1994, six surveillance sites were chosen based on an objective review of submitted proposals from state health departments, the data-collection instrument was formalized and pilot tested, and surveillance staff were hired and trained. Hemophilia case identification and data abstraction began in 1995. Information about case definitions, case-finding methods, and the data being abstracted can be found in the Technical Notes of this report.

The Hemophilia Surveillance System (HSS) is the first population-based study of hemophilia in the United States. Data from the medical records of more than 3,000 persons with hemophilia have been abstracted and entered into a computer database. The database will be an invaluable source of information needed to achieve the goal of reducing or preventing the complications of hemophilia.

The purpose of this surveillance report is to disseminate this information to public health workers, health educators and planners, and patients and care providers within the hemophilia community. This report extends the information provided in the first issue of this report about the

occurrence of hemophilia and about infection with HIV and mortality among persons with hemophilia residing in the surveillance states. Additionally, data about treatment product use, inhibitor history, and immune tolerance therapy is included in this issue. We hope that this information will prove useful to those involved in efforts to reduce or prevent the complications of this disease.

The proper interpretation and appropriate use of surveillance data require an understanding of how the data are collected, reported, and analyzed. Therefore, readers of this report are encouraged to review the Technical Notes, beginning on page 13.

Suggested Reading:

CDC. Hepatitis A among persons with hemophilia who received clotting factor concentrate - United States, September-December 1995. *MMWR* 1996;45:29-32.

CDC. Prevention of hepatitis A through active or passive immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 1996;45(No. RR-15):1-30.

CDC. Transmission of hepatitis C virus infection associated with home infusion therapy for hemophilia. *MMWR* 1997;46:597-599.

Information available from HANDI by calling (800-42-HANDI):

What You Should Know about Bleeding Disorders (1997)

Comprehensive Care for People with Hemophilia by Shelby Dietrich, MD (1991)

Understanding Hepatitis by Leonard Seeff, MD (1997)

HIV Disease in People with Hemophilia: Your Questions Answered by Glenn Pierce, MD, PhD (1991)

Bleeding Disorders and AIDS: The Facts (1997)

Table 1. Number of prevalent male cases of hemophilia A (HemA) and hemophilia B (HemB) identified in six U.S. states during 1993-1997

	1996		1997		1993-1997	
State of residence	HemA No.	HemB No.	HemA No.	HemB No.	HemA No.	HemB No.
Colorado	186	51	198	55	230	60
Georgia	419	91	442	95	516	108
Louisiana	194	82	191	85	224	87
Massachusetts	325	63	281	56	403	87
New York*	902	270	886	269	1105	312
Oklahoma	164	60	167	64	200	69
Total	**2190**	**617**	**2165**	**624**	**2678**	**723**

*One person had both hemophilia A and B and is included in both columns as a case for all years.

Table 2. Number of incident male cases of hemophilia A (HemA) and hemophilia B (HemB) identified in six U.S. states during 1993-1997

	1996		1997		1993-1997	
State of residence	HemA No.	HemB No.	HemA No.	HemB No.	HemA No.	HemB No.
All States**	24	8	38	6	175	47

**Note: The number of cases with birthdates in the year of the surveillance. This number will be an undercount of new cases of hemophilia because a diagnosis of hemophilia is often not made until the child is more than 5 years old, especially for children with mild cases of disease. Since these data were collected during 1994-1998, cases among persons born in 1993-1997 may not yet have been diagnosed.

Table 3. Age distribution of males with hemophilia residing in six U.S. states in 1996

Hemophilia Type		Age Group (years) 0- 4	5-	10-	15-	20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	75+	Total
A	N	207	291	246	260	167	183	186	157	136	122	57	46	45	35	23	29	2190
	%	9.4	13.3	11.2	11.9	7.6	8.4	8.5	7.2	6.2	5.6	2.6	2.1	2.0	1.6	1.0	1.3	
B	N	65	76	64	64	54	54	51	46	38	29	23	15	14	7	9	8	617
	%	10.5	12.3	10.4	10.4	8.8	8.8	8.3	7.5	6.2	4.7	3.7	2.4	2.3	1.1	1.5	1.3	

Table 4. Age distribution of males with hemophilia residing in six U.S. states in 1997

Hemophilia Type		Age Group (years) 0- 4	5-	10-	15-	20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	75+	Total
A	N	230	271	253	273	156	181	163	152	135	110	75	47	33	31	26	29	2165
	%	10.6	12.5	11.7	12.6	7.2	8.4	7.5	7.0	6.2	5.1	3.5	2.2	1.5	1.4	1.2	1.3	
B	N	59	78	68	63	55	47	55	53	39	28	26	14	15	9	5	10	624
	%	9.5	12.5	10.9	10.1	8.8	7.5	8.8	8.5	6.2	4.5	4.2	2.2	2.4	1.4	0.8	1.6	

Table 5. Age distribution of males with hemophilia residing in six U.S. states in 1993-1997

Hemophilia Type		Age Group* (years) 0- 4	5-	10-	15-	20-	25-	30-	35-	40-	45-	50-	55-	60-	65-	70-	75+	Total
A	N	250	291	276	305	209	237	233	206	179	147	104	62	52	46	35	46	2678
	%	9.3	10.9	10.3	11.4	7.8	8.8	8.7	7.7	6.7	5.5	3.9	2.3	1.9	1.7	1.3	1.7	
B	N	64	85	75	71	64	61	60	64	48	33	30	17	19	10	7	15	723
	%	8.8	11.8	10.4	9.8	8.8	8.4	8.3	8.8	6.6	4.6	4.2	2.4	2.6	1.4	1.0	2.1	

*Cases were assigned to an age group according to their age when first identified by the surveillance.

Table 6. Prevalent male cases of hemophilia A (HemA) and hemophilia B (HemB) identified in six U.S. states during 1993-1997 by race/ethnicity

	1996		1997		1993-1997	
Race/Ethnicity	HemA No.(%)	HemB No.(%)	HemA No.(%)	HemB No.(%)	HemA No.(%)	HemB No.(%)
White	1596 (72.9)	437 (70.8)	1554 (71.8)	447 (71.6)	1935 (72.3)	519 (71.8)
African-American	271 (12.4)	111 (18.0)	284 (13.1)	111 (17.8)	339 (12.7)	123 (17.0)
Hispanic	191 (8.7)	31 (5.0)	186 (8.6)	29 (4.6)	228 (8.5)	35 (4.8)
Native American	16 (0.7)	13 (2.1)	15 (0.7)	13 (2.1)	16 (0.6)	14 (1.9)
Mixed Race	26 (1.2)	9 (1.5)	29 (1.3)	10 (1.6)	32 (1.2)	10 (1.4)
Other*	58 (2.6)	7 (1.1)	64 (3.0)	8 (1.3)	72 (2.7)	10 (1.4)
Unknown/Missing	32 (1.5)	9 (1.5)	33 (1.5)	6 (1.0)	56 (2.1)	12 (1.7)
Total	**2190**	**617**	**2165**	**624**	**2678**	**723**

*Includes Asian/Pacific Islander

Table 7. Distribution of male hemophilia cases residing in six U.S. states in 1996 by severity level

Hemophilia Type		Severity Level* Mild	Moderate	Severe	Unknown	TOTAL
A	N	720	488	937	45	2190
	%	32.9	22.3	42.8	2.0	
B	N	183	204	208	22	617
	%	29.7	33.1	33.7	3.6	

Table 8. Distribution of male hemophilia cases residing in six U.S. states in 1997 by severity level

Hemophilia Type		Severity Level* Mild	Moderate	Severe	Unknown	TOTAL
A	N	709	494	916	46	2165
	%	32.8	22.8	42.3	2.1	
B	N	189	202	209	24	624
	%	30.3	32.4	33.5	3.8	

Table 9. Distribution of male hemophilia cases residing in six U.S. states in 1993-97 by severity level

Hemophilia Type		Severity Level* Mild	Moderate	Severe	Unknown	TOTAL
A	N	874	586	1148	70	2678
	%	32.6	21.9	42.9	2.6	
B	N	223	232	236	32	723
	%	30.8	32.1	32.6	4.4	

*Mild is factor activity (FA) 6%-30% of normal; Moderate is FA 1%-5% of normal; Severe is FA <1% of normal.

Table 10. Treatment product use by prevalent male cases of hemophilia A identified in six U.S. states during 1993-1997.

Product type	1993 (N=2134)	1994 (n=2179)	1995 (n=2215)	1996 (n=2200)	1997 (n=2172)
Recombinant	172 (8.1)	314 (14.4)	426 (19.2)	517 (23.5)	667 (30.7)
Monoclonal	814 (38.1)	727 (33.4)	634 (28.6)	511 (23.2)	402 (18.5)
Other	216 (10.1)	165 (7.6)	107 (4.8)	149 (6.8)	130 (6.0)
Porcine	17 (*)	9 (*)	9 (*)	8 (*)	2 (*)
Prothrombin Complex	38 (1.8)	41 (1.9)	40 (1.8)	29 (1.3)	23 (1.1)
Activated Complex	63 (3.0)	59 (2.7)	57 (2.6)	52 (2.4)	55 (2.5)
Cryoprecipitate/FFP**	***	***	***	34 (1.5)	31 (1.4)
Desmopressin	180 (8.4)	155 (7.1)	176 (7.9)	184 (8.4)	201 (9.3)
None	297 (13.9)	211 (9.7)	304 (13.7)	317 (14.4)	250 (11.5)

* < 1%
**FFP = Fresh frozen plasma
***Information on blood product use was not uniformly collected until 1996.
Note: Recombinant factor VIII product was licensed in December, 1992.

Does not total 100% due to missing information.

Table 11. Treatment product use by prevalent male cases of hemophilia B identified in six U.S. states during 1993-1997.

Product type	1993 (N=582)	1994 (n=608)	1995 (n=628)	1996 (n=617)	1997 (n=624)
Recombinant	0	0	0	10 (1.6)	62 (9.9)
Purified IX	130 (22.3)	193 (31.7)	218 (34.7)	223 (36.1)	218 (34.9)
Prothrombin Complex	165 (28.4)	129 (21.2)	109 (17.4)	74 (12.0)	42 (6.7)
Activated Complex	8 (1.4)	8 (1.3)	6 (1.0)	8 (1.3)	9 (1.4)
Cryoprecipitate/FFP**	***	***	***	13 (2.1)	6 (1.0)
None	101 (17.4)	99 (16.3)	108 (17.2)	111 (18.0)	95 (15.2)

* < 1%
**FFP = Fresh frozen plasma
***Information on blood product use was not uniformly collected until 1996.
Note: Recombinant factor IX product was licensed in February, 1997.

Does not total 100% due to missing information.

Table 12. Inhibitor history and current immune tolerance therapy (ITT) among prevalent hemophilia cases identified in six U.S. states, 1996.

	Severity Level*		
	Mild	Moderate	Severe
Hemophilia A	(N=487)	(N=402)	(N=867)
Ever inhibitor	10 (2.0)	28 (7.0)	189 (21.8)
Current ITT	1 (0.2)	2 (0.5)	48 (5.6)
Hemophilia B	(N=128)	(N=167)	(N=185)
Ever inhibitor	3 (2.3)	2 (1.2)	15 (8.1)
Current ITT	0	0	4 (2.2)

*Mild is factor activity (FA) 6%-30% of normal; Moderate is FA 1%-5% of normal; Severe is FA <1% of normal.

Table 13. Inhibitor history and current immune tolerance therapy (ITT) among prevalent hemophilia cases identified in six U.S. states, 1997.

	Severity Level*		
	Mild	Moderate	Severe
Hemophilia A	(N=499)	(N=425)	(N=854)
Ever inhibitor	9 (1.8)	28 (6.6)	175 (20.5)
Current ITT	0	3 (0.7)	38 (4.6)
Hemophilia B	(N=133)	(N=158)	(N=184)
Ever inhibitor	1 (0.8)	4 (2.5)	15 (8.2)
Current ITT	0	1 (0.7)	4 (2.2)

*Mild is factor activity (FA) 6%-30% of normal; Moderate is FA 1%-5% of normal; Severe is FA <1% of normal.

Table 14. HIV serostatus of prevalent male cases of hemophilia A and B identified in six U.S. states during 1993-1997

	1996		1997		1993-1997	
Ever Seropositive	No.	%	No.	%	No.	%
Yes	591	21.1	542	19.5	837	24.6
No	1345	47.9	1367	49.0	1827	53.7
Unknown/Missing*	870	31.0	879	31.5	736	21.6
Total	**2806**		**2788**		**3400**	

*Includes untested persons.

Table 15. AIDS cases among HIV-seropositive male hemophilia A and B cases during 1993-1997

	1996		1997		1993-1997	
AIDS Case	No.	%	No.	%	No.	%
Yes	170	28.8	163	30.1	363	43.4
No	376	63.6	333	61.4	411	49.1
Unknown	45	7.6	46	8.5	63	7.5
Total	**591**		**542**		**837**	

Table 16. Presence of AIDS indicator disease among HIV-seropositive males with hemophilia A and B identified in six U.S. states during 1993-1997

	1996		1997		1993-1997	
AIDS indicator disease	No.	%	No.	%	No.	%
Yes	25	4.2	15	2.8	74	8.8
No	566	95.8	527	97.2	763	91.2
Total	**591**		**542**		**837**	

Table 17. Annual crude mortality among males with hemophilia A or B identified in six U.S. states during 1993-1997

	1996		1997		1993-1997	
End of year vital status	No.	%	No.	%	No.	%
Alive	2475	98.0	2496	98.3	2694	88.8
Deceased	50	2.0	42	1.7	339	11.2
Total*	**2525**		**2538**		**3033**	

*Excludes cases among persons whose vital status was not known (persons who were lost to follow-up).

Technical Notes

Surveillance Definitions

A definitive hemophilia case was defined as a person with physician-diagnosed hemophilia A or B and a baseline clotting factor activity level of ≤ 30%. A presumptive hemophilia case was defined as a person with a physician diagnosis of hemophilia A or B for whom no measurement of factor VIII or IX activity level was available in the medical record. Persons with factor activity levels >30% of normal, acquired inhibitors of factor VIII or IX, and carriers of the hemophilia gene were excluded. All tables include both presumptive and definitive cases. Severity level was categorized as mild if the activity level was 6%-30%, moderate if 1%-5%, and severe if <1% of normal. In cases with more than one available measurement of factor activity level, the lowest value was used to determine severity.

Because cases were identified primarily through contacts with the medical care system and since medical care visits did not occur in every year of the surveillance, cases were assigned a study status according to the following guidelines. Cases among persons who had a medical care visit at any time during the calendar year were considered "active." Those who did not have a medical care visit during the calendar year but whose residence and vital status could be verified in some other way were considered "inactive." Cases among persons with no medical visit and no verification of residence or vital status were considered "lost." These cases were assumed to be residents of the state for up to 5 years after their last medical care visit. After that time, cases with "lost" status were no longer counted as resident cases. Cases among persons who were known to have moved out of the surveillance state were listed as "transferred" in the year *after* they moved. Therefore, cases were counted as long as they were residents of a surveillance state for any part of a calendar year.

Age was calculated based on the first day of the year after the current surveillance year. This was done so that incident cases would not have an age less than zero. Information on race or ethnicity was obtained from medical records and may have been based either on self-report or on observations made by care providers.

Data on all clotting factor products, blood products, or other therapeutics prescribed during the year were abstracted from medical records. An individual was determined to have a positive history of antibodies (inhibitors) to clotting factor when the diagnosis, made at any time during his lifetime, was present in the medical record. A person was determined to have undergone immune tolerance therapy during the current abstract year when evidence of immune tolerance induction or maintenance therapy was present in medical records for that year.

Cases were considered to be seropositive for HIV if information in their medical record indicated that the person had ever tested positive for HIV-1 antibody. Similarly, cases were considered seronegative based on evidence of a negative test for HIV-1 antibody. Cases for whom no evidence of HIV-1 antibody testing could be found were categorized as having unknown HIV status.

Among persons with hemophilia who were HIV-1 seropositive, cases were considered to have AIDS if information available in the medical record indicated that they met the CDC surveillance case definition for AIDS (*MMWR* 1987;36[no. 1S]: 3S-15S. For surveillance of AIDS-indicator diseases, those diseases listed in the surveillance case definition were considered.

Data collection and quality control

Cases were identified using a wide variety of approaches that utilized resources available to the health departments of the surveillance states. These methods included contacting hematologists and other physicians, clinical laboratories, hemophilia treatment centers, factor concentrate suppliers, pharmacies, and other potential providers of care or supplies for this population. In some states, databases such as hospital-discharge records and Medicare claims data were reviewed. The completeness of case ascertainment was evaluated in each state using several formal and informal strategies.

Once cases were identified, trained data abstractors collected data using standardized data collection forms. Project staff were trained by CDC personnel and were provided with a detailed procedures manual. Specific questions about data abstraction that arose during the project were addressed by CDC epidemiologic support staff who also monitored the progress of data collection and made periodic site visits to evaluate facilities, assess procedures, and meet with health department and surveillance staff to discuss local issues and concerns.

Information from all medical care encounters during the year was aggregated prior to entry into a computerized database using software that required double-key entry to limit the number of data-entry errors.

Data stored in local databases were periodically transmitted without patient identifiers to CDC for analysis. All transmitted data were screened for omissions, inconsistencies, and unusual values that possibly represented abstraction or data-entry errors. Data queries were electronically transmitted to the data collection site and study staff used available information to resolve discrepancies and to update the database as necessary.

Tabulation and presentation of data

Data in this report are provisional. This issue extends the information provided in the first surveillance report to cover the 4th and 5th years of a 6-year surveillance project. In addition, this report includes information on the type of clotting factor, blood product, or other treatment product prescribed for the patient during the year as well as data concerning inhibitors and current immune tolerance therapy.

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